Status: Path 1 of [Di[redacted]g Information Services via Mode[redacted]

Status: Initializing TCP/IP using (UseTelnetProto 1 ServiceID pto-dialog)
Trying 3106900061...Open

DIALOG INFORMATION SERVICES
PLEASE LOGON:
 ******** HHHHHHHH SSSSSSS?
Status: Signing onto Dialog
 ****
ENTER PASSWORD:
 ******** HHHHHHHH SSSSSSS? ********
Welcome to DIALOG
Status: Connected

Dialog level 01.10.01D

Last logoff: 25oct01 12:53:29
Logon file405 26oct01 12:18:56
           *** ANNOUNCEMENT ***
                    ***
--Important Notice to Freelance Authors--
See HELP FREELANCE for more information
                    ***
NEW FILES RELEASED
***Disclosure Database (File 101)
***Harris Business Profiler (File 537)
***Mergent Company Profiles (File 555)
***Mergent Company Snapshots (File 556)
***Mergent Company News Reports (File 557)
***Financial Times Fulltext (File 476)

***TRADEMARKSCAN-Japan (File 669)

UPDATING RESUMED
***Delphes European Business (File 481)
***Books In Print (File 470)
                    ***
RELOADED
***CLAIMS/US PATENTS (Files 340, 341, 942)
***Kompass Middle East/Africa/Mediterranean (File 585)
***Kompass Asia/Pacific (File 592)
***Kompass Central/Eastern Europe (File 593)
***Kompass Canada (File 594)
***CANCERLIT (File 159)
***Information Science Abstracts (File 202)

New document supplier
IMED has been changed to INFOTRIE (see HELP OINFOTRI)

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   broad spectrum of news wires.

     >>> Enter BEGIN HOMEBASE for Dialog Announcements <<<
     >>>   of new databases, price changes, etc.   <<<
                    ****
KWIC is set to 50.
HILIGHT set on as '*'
PICKS is set ON as an alias for 5,55,159,143,358,340,344,348,351,352,447,72,73,154,1

55,349.
.
SYSTEM:HOME
Cost is in DialUnits
Menu System II: D2 version 1.7.8 term=ASCII
*** DIALOG HOMEBASE(SM) Main Menu ***

Information:
1. Announcements (new files, reloads, etc.)
2. Database, Rates, & Command Descriptions
3. Help in Choosing Databases for Your Topic
4. Customer Services (telephone assistance, training, seminars, etc.)
5. Product Descriptions

Connections:
6. DIALOG(R) Document Delivery
7. Data Star(R)

/H = Help /L = Logoff /NOMENU = Command Mode

Enter an option number to view information or to connect to an online service. Enter a BEGIN command plus a file number to search a database (e.g., B1 for ERIC).
?b picks

>>> 351 is unauthorized
>>> 352 is unauthorized
>>>2 of the specified files are not available
26oct01 12:19:18 User243038 Session D84.1
$0.00 0.207 DialUnits FileHomeBase
$0.00 Estimated cost FileHomeBase
$0.02 TYMNET
$0.02 Estimated cost this search
$0.02 Estimated total session cost 0.207 DialUnits

SYSTEM:OS - DIALOG OneSearch
File 5:Biosis Previews(R) 1969-2001/Oct W3
(c) 2001 BIOSIS
File 55:Biosis Previews(R) 1993-2001/Oct W3
(c) 2001 BIOSIS
File 159:Cancerlit 1975-2001/Sep
(c) format only 2001 Dialog Corporation
File 143:Biol. & Agric. Index 1983-2001/Sep
(c) 2001 The HW Wilson Co
File 358:Current BioTech Abs 1983-2001/Sep
(c) 2001 DECHEMA
***File 358: Updates delayed. Please see HELP NEWS 358 for details.**
File 340:CLAIMS(R)/US PATENT 1950-01/Oct 16
(c) 2001 IFI/CLAIMS(R)
***File 340: has been reloaded. Published applications are available.**
See HELP NEWS 340 for details.
File 344:CHINESE PATENTS ABS APR 1985-2001/Sep
(c) 2001 EUROPEAN PATENT OFFICE
File 348:EUROPEAN PATENTS 1978-2001/Oct W02
(c) 2001 European Patent Office
File 447:IMSWorld Patents International 2001/Sep
(c) 2001 IMSWorld Publ. Ltd.
File 72:EMBASE 1993-2001/Oct W3
(c) 2001 Elsevier Science B.V.
***File 72: For information about Explode feature please**
see Help News72.
File 73:EMBASE 1974-2001/Oct W3
(c) 2001 Elsevier Science B.V.

```
*File  73: For information about Explode feature please
see Help News73.
  File 154:Medline(R)  1990-2001/Nov W3
  File 155:MEDLINE(R)  1966-2001/Nov W3
  File 349:PCT Fulltext  1983-2001/UB=20011018,UT=20011011
        (c) 2001 WIPO/Univentio
*File 349: Additional fulltext records and images will be added
shortly.  Additional coverage added. See HELP NEWS 349.

      Set  Items  Description
      ---  -----  -----------
?s e-cadherin
      S1    3306  E-CADHERIN
?s s1 and endothelin B receptor
            3306  S1
            4105  ENDOTHELIN B RECEPTOR
      S2       0  S1 AND ENDOTHELIN B RECEPTOR
?s  catenin?
      S3   16499  CATENIN?
?s s3 and s1
           16499  S3
            3306  S1
      S4    1160  S3 AND S1
?s endothelin B receptor
      S5    4105  ENDOTHELIN B RECEPTOR
?s s5 and s4
            4105  S5
            1160  S4
      S6       0  S5 AND S4
?ds

Set     Items   Description
S1       3306   E-CADHERIN
S2          0   S1 AND ENDOTHELIN B RECEPTOR
S3      16499   CATENIN?
S4       1160   S3 AND S1
S5       4105   ENDOTHELIN B RECEPTOR
S6          0   S5 AND S4
?s s1 and cancer?
            3306  S1
         2982891  CANCER?
      S7    1040  S1 AND CANCER?
?s s7 and s5
            1040  S7
            4105  S5
      S8       0  S7 AND S5
?s s7 and endothelian antagonist?
            1040  S7
               0  ENDOTHELIAN ANTAGONIST?
      S9       0  S7 AND ENDOTHELIAN ANTAGONIST?
?ds

Set     Items   Description
S1       3306   E-CADHERIN
S2          0   S1 AND ENDOTHELIN B RECEPTOR
S3      16499   CATENIN?
S4       1160   S3 AND S1
S5       4105   ENDOTHELIN B RECEPTOR
S6          0   S5 AND S4
S7       1040   S1 AND CANCER?
S8          0   S7 AND S5
S9          0   S7 AND ENDOTHELIAN ANTAGONIST?
?s sy and treat?
Processing
Processed  10 of  14 files ...
Completed processing all files
           10272  SY
```

```
        8141373  TREAT?
     S10    3690  SY AND TREAT?
?s s7 and treat?
            1040  S7
         8141373  TREAT?
     S11     132  S7 AND TREAT?
?ds

Set     Items   Description
S1       3306   E-CADHERIN
S2          0   S1 AND ENDOTHELIN B RECEPTOR
S3      16499   CATENIN?
S4       1160   S3 AND S1
S5       4105   ENDOTHELIN B RECEPTOR
S6          0   S5 AND S4
S7       1040   S1 AND CANCER?
S8          0   S7 AND S5
S9          0   S7 AND ENDOTHELIAN ANTAGONIST?
S10      3690   SY AND TREAT?
S11       132   S7 AND TREAT?
?s s11 and BQ788
             132  S11
             901  BQ788
     S12       0  S11 AND BQ788
?s BQ788
     S13     901  BQ788
?s s13 and s1
             901  S13
            3306  S1
     S14       0  S13 AND S1
?s s13 and s3
             901  S13
           16499  S3
     S15       1  S13 AND S3
?t s15/5/all

 15/5/1     (Item 1 from file: 349)
DIALOG(R)File 349:PCT Fulltext
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00754503
CANCER TREATMENT WITH ENDOTHELIN RECEPTOR ANTAGONISTS
THERAPIE  ANTICANCEREUSE  FAISANT  APPEL A DES ANTAGONISTES DU RECEPTEUR DE
   L'ENDOTHELINE
Patent Applicant/Assignee:
  NEW YORK UNIVERSITY, 550 First Avenue, New York, NY 10016, US, US
    (Residence), US (Nationality)
Inventor(s):
  SCHNEIDER Robert J, Apartment 15M, 70 East 10th Street, New York, NY
    10003, US
  JAMAL Sumayah, 24 Gramercy Park, South, New York, NY 10003, US
Legal Representative:
  CORUZZI Laura A, Pennie & Edmonds LLP, 1155 Avenue of the Americas, New
    York, NY 10036, US
Patent and Priority Information (Country, Number, Date):
  Patent:               WO 200067024 A1 20001109 (WO 0067024)
  Application:          WO 2000US11990 20000503  (PCT/WO US0011990)
  Priority Application: US 99305084 19990504
Designated States: AE AG AL AM AT AU AZ BA BB BG BR BY CA CH CN CR CU CZ DE
  DK DM DZ EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC
  LK LR LS LT LU LV MA MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK
  SL TJ TM TR TT TZ UA UG UZ VN YU ZA ZW
  (EP) AT BE CH CY DE DK ES FI FR GB GR IE IT LU MC NL PT SE
  (OA) BF BJ CF CG CI CM GA GN GW ML MR NE SN TD TG
  (AP) GH GM KE LS MW SD SL SZ TZ UG ZW
  (EA) AM AZ BY KG KZ MD RU TJ TM
Main International Patent Class: G01N-033/53
```

International Patent Clas[redacted]G01N-033/567; A01N-037/18; A61[redacted]38/00;
C07K-014/00; C07K-016/00; C07K-017/00; C07K-002/00; C07K-[redacted]4/00;
C07K-005/00; C07K-007/00
Publication Language: English
Filing Language: English
Fulltext Availability:
Detailed Description
Claims
Fulltext Word Count: 21420

English Abstract
The present invention relates to therapeutic protocols and pharmaceutical compositions designed to treat and prevent cancer. More specifically, the present invention relates to a novel method of treating cancer using antagonists to the endothelin B receptor (ETB) or inactive mimic forms of endothelin-1. The pharmaceutical compositions of the invention are capable of selectively inhibiting the early events associated with the development of cancer. The present invention further relates to screening assays to identify compounds which inhibit ETB activation.

French Abstract
La presente invention concerne des protocoles therapeutiques et des compositions pharmaceutiques destines a traiter et prevenir le cancer. L'invention se rapporte, en particulier, a un nouveau procede permettant de traiter le cancer a l'aide d'antagonistes du recepteur de l'endotheline B (ETB) ou a des formes mimetiques inactives de l'endotheline 1. Les compositions pharmaceutiques de l'invention sont capables d'inhiber selectivement les evenements precoces associes au developpement du cancer. L'invention concerne en outre des analyses de criblage permettant d'identifier des composes qui inhibent l'activation de l'ETB.

Legal Status (Type, Date, Text)
Publication 20001109 A1 With international search report.
Publication 20001109 A1 Before the expiration of the time limit for amending the claims and to be republished in the event of the receipt of amendments.
Examination 20010802 Request for preliminary examination prior to end of 19th month from priority date
?ds

Set	Items	Description
S1	3306	E-CADHERIN
S2	0	S1 AND ENDOTHELIN B RECEPTOR
S3	16499	CATENIN?
S4	1160	S3 AND S1
S5	4105	ENDOTHELIN B RECEPTOR
S6	0	S5 AND S4
S7	1040	S1 AND CANCER?
S8	0	S7 AND S5
S9	0	S7 AND ENDOTHELIAN ANTAGONIST?
S10	3690	SY AND TREAT?
S11	132	S7 AND TREAT?
S12	0	S11 AND BQ788
S13	901	BQ788
S14	0	S13 AND S1
S15	1	S13 AND S3

?s s7 and endothelin
1040 S7
88708 ENDOTHELIN
S16 0 S7 AND ENDOTHELIN
?s s7 and endothelin receptor?
1040 S7
7609 ENDOTHELIN RECEPTOR?
S17 0 S7 AND ENDOTHELIN RECEPTOR?
?s s7 and treat?
1040 S7

```
        8141373  TREAT?
     S18     132  S7 AND TREAT?
?s s18 and melanoma
             132  S18
          252301  MELANOMA
     S19       4  S18 AND MELANOMA
?rd
>>>Duplicate detection is not supported for File 340.
>>>Duplicate detection is not supported for File 344.
>>>Duplicate detection is not supported for File 348.
>>>Duplicate detection is not supported for File 447.
>>>Duplicate detection is not supported for File 349.

>>>Records from unsupported files will be retained in the RD set.
...completed examining records
     S20       2  RD (unique items)
?t s20/5/all
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20/5/1 (Item 1 from file: 5)

13076400 BIOSIS NO.: 200100283549

The addition of bisecting N-acetylglucosamine residues to E-cadherin down-regulates the tyrosine phosphorylation of beta-catenin.

AUTHOR: Kitada Takatoshi; Miyoshi Eiji; Noda Katsuhisa; Higashiyama Shigeki ; Ihara Hideyuki; Matsuura Nariaki; Hayashi Norio; Kawata Sumio; Matsuzawa Yuji; Taniguchi Naoyuki(a)
AUTHOR ADDRESS: (a)Department of Biochemistry, Osaka University Graduate School of Medicine, 2-2 Yamadaoka, Suita, Osaka, 565-0871: proftani@biochem.med.osaka-u.ac.jp**Japan

JOURNAL: Journal of Biological Chemistry 276 (1):p475-480 January 5, 2001
MEDIUM: print
ISSN: 0021-9258
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English
SUMMARY LANGUAGE: English

ABSTRACT: The enzyme GnT-III (beta1,4-N-acetylglucosaminyltransferase III) catalyzes the addition of a bisecting N-acetylglucosamine (GlcNAc) residue on glycoproteins. Our previous study described that the transfection of GnT-III into mouse *melanoma* cells results in the enhanced expression of E-cadherin, which in turn leads to the suppression of lung metastasis. It has recently been proposed that the phosphorylation of a tyrosine residue of beta-catenin is associated with cell migration. The present study reports on the importance of bisecting GlcNAc residues by GnT-III on tyrosine phosphorylation of beta-catenin using three types of *cancer* cell lines. An addition of bisecting GlcNAc residues to E-cadherin leads to an alteration in cell morphology and the localization of beta-catenin after epidermal growth factor stimulation. These changes are the result of a down-regulation in the tyrosine phosphorylation of beta-catenin. In addition, tyrosine phosphorylation of beta-catenin by transfection of constitutively active c-src was suppressed in GnT-III transfectants as well as in the case of epidermal growth factor stimulation. *Treatment* with tunicamycin abolished any differences in beta-catenin phosphorylation for the mock vis a vis the GnT-III transfectants. Thus, the addition of a specific N-glycan structure, the bisecting GlcNAc to E-cadherin-beta-catenin complex, down-regulates the intracellular signaling pathway, suggesting its implication in cell motility and the suppression of *cancer* metastasis.

DESCRIPTORS:
MAJOR CONCEPTS: Biochemistry and Molecular Biophysics; Methods and Techniques
BIOSYSTEMATIC NAMES: Hominidae--Primates, Mammalia, Vertebrata, Chordata, Animalia; Muridae--Rodentia, Mammalia, Vertebrata, Chordata, Animalia

ORGANISMS: B16-hm cell line (Muridae)--mouse *melanoma* cell; Huh7 cell line (Hominidae)--human hepatoma cell; WiDr cell line (Hominidae)--human colon *cancer* cell
BIOSYSTEMATIC CLASSIFICATION (SUPER TAXA): Animals; Chordates; Humans; Mammals; Nonhuman Mammals; Nonhuman Vertebrates; Primates; Rodents; Vertebrates
DISEASES: lung metastasis--neoplastic disease, respiratory system disease ; *melanoma*--neoplastic disease
CHEMICALS & BIOCHEMICALS: *E-cadherin*; beta-catenin--down-regulation, tyrosine phosphorylation; bisecting N-acetylglucosamine residues--addition
MISCELLANEOUS TERMS: *cancer* metastasis--suppression; cell motility
ALTERNATE INDEXING: Lung Neoplasms (MeSH); *Melanoma* (MeSH)
CONCEPT CODES:
10060 Biochemical Studies-General
02506 Cytology and Cytochemistry-Animal
02508 Cytology and Cytochemistry-Human
10064 Biochemical Studies-Proteins, Peptides and Amino Acids
16006 Respiratory System-Pathology
24004 Neoplasms and Neoplastic Agents-Pathology; Clinical Aspects; Systemic Effects
BIOSYSTEMATIC CODES:
86215 Hominidae
86375 Muridae

20/5/2 (Item 2 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

13057497 BIOSIS NO.: 200100264646
Tumor heterogeneity and tumor cell-extracellular matrix interactions are essential for the development of patterned tubular intratumoral channels in aggressive prostate *cancer*.
AUTHOR: Sharma Navesh(a); Seftor Richard E B(a); Lubaroff David M(a); Heidger Paul M(a); Hendrix Mary J C(a)
AUTHOR ADDRESS: (a)University of Iowa College of Medicine, 51, Newton Road, Iowa City, IA, 52242**USA
JOURNAL: FASEB Journal 15 (5):pA1078 March 8, 2001
MEDIUM: print
CONFERENCE/MEETING: Annual Meeting of the Federation of American Societies for Experimental Biology on Experimental Biology 2001 Orlando, Florida, USA March 31-April 04, 2001
ISSN: 0892-6638
RECORD TYPE: Abstract
LANGUAGE: English
SUMMARY LANGUAGE: English

ABSTRACT: The in situ formation of primitive vascular networks in uveal *melanoma*- a phenomenon involving the formation of patterned networks by tumor cells in 3-D cultures which "mimic" patterned networks formed during embryonic vasculogenesis, has been termed tumor cell vasculogenesis. Our results utilizing rat prostate tumors and neoplastic prostate cell lines strongly support the concept that "vasculogenic mimicry" is exhibited by aggressive, but not nonaggressive, prostate neoplasms. The tubular networks formed by aggressive rat and human prostate *cancer* cell lines are lined by desmosomally connected cells, conduct dyes reminiscent of microvascular circulation networks, and express various matrix metalloproteinases and vascular markers. Green fluorescent protein labeling of individual clonal rat cell populations reveals the requirement of the E-cadherin positive, R3327-5'B cells along the tubular linings, while the fibroblast-like cell populations (R3327-5'A or R3327-5'C) form the supporting architecture, suggesting compartmentalized roles for individual tumor cell populations. The presence of these channelized networks in vivo coincides with a lack of tumor necrosis and occurs in close proximity to conventional endothelial lined vasculature. Aggressive prostate tumor cells possess the ability to

contract floating collagen gels, indicative of their biomechanical remodeling ability. Individual populations also secrete angiogenic factors and express vascular markers that could facilitate both angiogenesis and vasculogenic mimicry. Channeled tubular network formation in 3-D matrices and contraction of floating collagen gels can be abrogated using CMT-3, an inhibitor or matrix metalloproteinase function. Additionally, these networks express the alpha6beta1 laminin receptor, demonstrate laminin expression, and can be disrupted using a laminin-blocking antibody. These results elucidate key mechanisms involved in tumor cell vasculogenic mimicry, and help illustrate how aggressive tumor cells mimic other cell types as they remodel their environment, providing novel prognostic markers and *treatment* strategies.

REGISTRY NUMBERS: 141907-41-7: MATRIX METALLOPROTEINASES
DESCRIPTORS:
  MAJOR CONCEPTS: Cardiovascular System (Transport and Circulation); Tumor Biology
  BIOSYSTEMATIC NAMES: Muridae--Rodentia, Mammalia, Vertebrata, Chordata, Animalia
  ORGANISMS: rat (Muridae)
  ORGANISMS: PARTS ETC: B cell--blood and lymphatics, immune system; vascular networks--circulatory system
  BIOSYSTEMATIC CLASSIFICATION (SUPER TAXA): Animals; Chordates; Mammals; Nonhuman Mammals; Nonhuman Vertebrates; Rodents; Vertebrates
  DISEASES: prostate *cancer*--neoplastic disease, reproductive system disease/male, urologic disease; uveal *melanoma*--eye disease, neoplastic disease
  CHEMICALS & BIOCHEMICALS: CMT-1; *E-cadherin*; alpha-6-beta-1--laminin receptor; matrix metalloproteinases
  MISCELLANEOUS TERMS: embryonic vasculogenesis; tumor cell vasculogenesis; tumor cell-extracellular matrix interactions; tumor heterogeneity; Meeting Abstract
ALTERNATE INDEXING: Prostatic Neoplasms (MeSH); Uveal Neoplasms (MeSH)
CONCEPT CODES:
  02506 Cytology and Cytochemistry-Animal
  00520 General Biology-Symposia, Transactions and Proceedings of Conferences, Congresses, Review Annuals
  10064 Biochemical Studies-Proteins, Peptides and Amino Acids
  10802 Enzymes-General and Comparative Studies; Coenzymes
  14504 Cardiovascular System-Physiology and Biochemistry
  15002 Blood, Blood-Forming Organs and Body Fluids-Blood and Lymph Studies
  15004 Blood, Blood-Forming Organs and Body Fluids-Blood Cell Studies
  15506 Urinary System and External Secretions-Pathology
  16506 Reproductive System-Pathology
  20006 Sense Organs, Associated Structures and Functions-Pathology
  24003 Neoplasms and Neoplastic Agents-Immunology
  24004 Neoplasms and Neoplastic Agents-Pathology; Clinical Aspects; Systemic Effects
  34502 Immunology and Immunochemistry-General; Methods
  34508 Immunology and Immunochemistry-Immunopathology, Tissue Immunology
BIOSYSTEMATIC CODES:
  86375 Muridae
?ds

Set	Items	Description
S1	3306	E-CADHERIN
S2	0	S1 AND ENDOTHELIN B RECEPTOR
S3	16499	CATENIN?
S4	1160	S3 AND S1
S5	4105	ENDOTHELIN B RECEPTOR
S6	0	S5 AND S4
S7	1040	S1 AND CANCER?
S8	0	S7 AND S5
S9	0	S7 AND ENDOTHELIAN ANTAGONIST?
S10	3690	SY AND TREAT?

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S11       132   S7 AND TR[redacted]?
S12         0   S11 AND BQ[redacted]8
S13       901   BQ788
S14         0   S13 AND S1
S15         1   S13 AND S3
S16         0   S7 AND ENDOTHELIN
S17         0   S7 AND ENDOTHELIN RECEPTOR?
S18       132   S7 AND TREAT?
S19         4   S18 AND MELANOMA
S20         2   RD (unique items)
?s s18 and downregulation
            132  S18
          42087  DOWNREGULATION
     S21      6  S18 AND DOWNREGULATION
?rd
>>>Duplicate detection is not supported for File 340.
>>>Duplicate detection is not supported for File 344.
>>>Duplicate detection is not supported for File 348.
>>>Duplicate detection is not supported for File 447.
>>>Duplicate detection is not supported for File 349.

>>>Records from unsupported files will be retained in the RD set.
...completed examining records
     S22      3  RD (unique items)
?t s22/5/all

 22/5/1     (Item 1 from file: 5)
DIALOG(R)File   5:Biosis Previews(R)
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13117806   BIOSIS NO.:'200100324955
```

Transforming growth factor-beta1 promotes invasiveness after cellular transformation with activated Ras in intestinal epithelial cells.

AUTHOR: Fujimoto Koji; Sheng Hongmiao; Shao Jinyi; Beauchamp R Daniel(a)
AUTHOR ADDRESS: (a)Department of Surgery, Vanderbilt University Medical Center, 1161 21st Avenue South, CC-2306 Medical Center North, Nashville, TN, 37232-2279: daniel.beauchamp@mcmail.vanderbilt.edu**USA

JOURNAL: Experimental Cell Research 266 (2):p239-249 June 10, 2001
MEDIUM: print
ISSN: 0014-4827
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English
SUMMARY LANGUAGE: English

ABSTRACT: Invasion is a defining event in carcinoma progression. In general, invasive carcinoma is characterized by an epithelial-fibroblastoid conversion associated with loss of cell-cell adhesion receptors such as E-cadherin and beta-catenin. We report here that TGF-beta1 promotes the invasiveness by modulating the alterations of cellular plasticity including a loss of cell-cell contact in Ras-transformed epithelial cells. In order to examine the role of TGF-beta1 in the Ras-induced responses, intestinal epithelial cells expressing a conditionally activated Ha-RasVal12 (RIE-iRas cells) were used in this study. Induced expression of activated Ha-RasVal12 caused morphologic transformation of the RIE-iRas cells with an increase in vimentin expression and a decrease of E-cadherin levels. There was also redistribution of beta-catenin from the cytoplasm to the nucleus after the induction of Ras. TGF-beta1 *treatment* enhanced both the decrease in E-cadherin levels and the redistribution of beta-catenin. Interestingly, the activation of Ras markedly decreased the level of TGF-beta receptor type II (TbetaRII) in RIE-iRas cells. However, the expression of plasminogen activator inhibitor-1, which is known to be transcriptionally induced by TGF-beta1, was strongly induced by TGF-beta1 despite the marked *downregulation* of TbetaRII. The induction of Ha-RasVal12 markedly increased the invasiveness in RIE-iRas cells, as evaluated by a collagen type I-coated Boyden-chamber assay, and the Ras-mediated

invasiveness was signifi[redacted]ntly enhanced by TGF-beta1 *tre[redacted]ment*. Expression of a dominant [redacted]egative form of TbetaRII in the [redacted]IE-iRas cells abrogated both growth-inhibitory and invasion responses to TGF-beta1. Collectively, these results suggest that TGF-beta1 and oncogenic Ras collaborate in promoting cellular invasiveness in intestinal epithelial cells. The enhancement of invasiveness was correlated with decreased E-cadherin levels and subcellular distribution of beta-catenin. The enhancement of oncogenic Ras-mediated cell transformation by TGF-beta1 occurs via TbetaRII.

DESCRIPTORS:
MAJOR CONCEPTS: Biochemistry and Molecular Biophysics; Cell Biology; Digestive System (Ingestion and Assimilation); Tumor Biology
BIOSYSTEMATIC NAMES: Muridae--Rodentia, Mammalia, Vertebrata, Chordata, Animalia
ORGANISMS: RIE-iRas (Muridae)--rat intestinal epithelial cells
BIOSYSTEMATIC CLASSIFICATION (SUPER TAXA): Animals; Chordates; Mammals; Nonhuman Mammals; Nonhuman Vertebrates; Rodents; Vertebrates
DISEASES: colorectal *cancer*--digestive system disease, neoplastic disease
CHEMICALS & BIOCHEMICALS: *E-cadherin*; activated Ras; beta-catenin; transforming growth factor-beta receptor type II; transforming growth factor-beta-1
MISCELLANEOUS TERMS: cellular transformation; tumor invasiveness
ALTERNATE INDEXING: Colorectal Neoplasms (MeSH)
CONCEPT CODES:
10060 Biochemical Studies-General
02502 Cytology and Cytochemistry-General
02506 Cytology and Cytochemistry-Animal
10064 Biochemical Studies-Proteins, Peptides and Amino Acids
14004 Digestive System-Physiology and Biochemistry
14006 Digestive System-Pathology
17002 Endocrine System-General
24004 Neoplasms and Neoplastic Agents-Pathology; Clinical Aspects; Systemic Effects
BIOSYSTEMATIC CODES:
86375 Muridae

22/5/2 (Item 2 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

12819155 BIOSIS NO.: 200100026304
Androgen deprivation induces selective outgrowth of aggressive hormone-refractory prostate *cancer* clones expressing distinct cellular and molecular properties not present in parental androgen-dependent *cancer* cells.
AUTHOR: Tso Cho-Lea; McBride William H; Sun Jirong; Patel Belur; Tsui Ke-Hung; Paik Sun H; Gitlitz Barbara; Caliliw Randy; van Ophoven Arndt; Wu Lily; deKernion Jean; Belldegrun Arie(a)
AUTHOR ADDRESS: (a)Department of Urology, UCLA School of Medicine, CHS 66-118, Los Angeles, CA, 90095-1738**USA
JOURNAL: Cancer Journal 6 (4):p220-233 July-August, 2000
MEDIUM: print
ISSN: 1528-9117
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English
SUMMARY LANGUAGE: English

ABSTRACT: PURPOSE The mechanism of progression of human prostate *cancer* (CaP) cells under androgen ablation therapy remains unclear. To study the alternative pathways of CaP cell growth under conditions of androgen deprivation, androgen-independent CaP variants were selected and expanded from an androgen-dependent CaP line via an in vitro androgen deprivation *treatment*. Cellular and molecular properties of these

androgen-independent variants were characterized both in vitro and in vivo and compared with those of their parental androgen-dependent cells. METHODS Androgen deprivation *treatment* of an androgen-dependent CaP cell line, LNCaP, was carried out by replacing culture medium with RPMI 1640 medium plus 10% charcoal-stripped serum. Cells that survived through the androgen deprivation *treatment* were harvested and expanded in the androgen-deficient culture medium and were designated CL-1. The CL-1 cells were also recultured in androgen-containing medium and designated CL-2. The growth (cell cycle analysis, 3H-thymidine incorporation assay, growth expansion, and colonization efficiency), expression of CaP-associated markers (semiquantitative reverse transcriptase polymerase chain reaction), interaction with endothelial and bone marrow stromal cells, sensitivity to anticancer agents and radiation (growth inhibition), and tumorigenicity of CL-1 and CL-2 cells were determined and compared with these characteristics in parental LNCaP cells. RESULTS CL-1 and CL-2 cells are fast-growing cells when compared with parental LNCaP cells. They were capable of potentiating the growth of endothelial and bone marrow stromal cells in co-culture experiments and acquired significant resistance to radiation and to anticancer cytotoxic agents (Taxol(R) paclitaxel, vinblastine, and etoposide). In contrast to the poorly tumorigenic parental LNCaP cells, CL-1 and CL-2 lines proved highly tumorigenic, exhibiting invasive and metastatic characteristics in intact and castrated mice or in female mice within a short period of 3 to 4 weeks. No growth supplements (e.g., Matrigel) were needed. When transfected with the green fluorescence protein (GFP) gene and transplanted orthotopically in the accessory sex gland, extensive metastatic disease from the primary CL tumor could be identified in bone, lymph nodes, lung, liver, spleen, kidney, and brain. Semiquantitative reverse transcriptase polymerase chain reaction analysis revealed a markedly distinct molecular expression profile in the CL lines: overexpression of basic fibroblast growth factor, interleukin-6, interleukin-8, vascular endothelial growth factor, transforming growth factor-beta, epidermal growth factor receptor, caveolin, and bcl-2 messenger RNAs and marked down-regulation of E-cadherin, p-53, and pentaerythritol tetranitrate. CONCLUSIONS Early administration of hormonal therapy after failure of first line *treatment* is associated with a profound clonal selection of aggressive Al variants, such as CL-1 and CL-2 lines. These tumor lines, with their parental counterparts, can serve as valuable tools for studying the cellular and molecular mechanisms of CaP progression and metastasis under hormonal therapy. CL-1 and CL-2 offer a unique and reproducible model for the evaluation of drug sensitivity and for other therapeutic modalities for advanced prostate *cancer*.

REGISTRY NUMBERS: 106096-93-9: BASIC FIBROBLAST GROWTH FACTOR; 33419-42-0: ETOPOSIDE; 33069-62-4: PACLITAXEL; 33069-62-4: TAXOL; 78-11-5: PENTAERYTHRITOL TETRANITRATE; 127464-60-2: VASCULAR ENDOTHELIAL GROWTH FACTOR; 865-21-4: VINBLASTINE

DESCRIPTORS:

MAJOR CONCEPTS: Molecular Genetics (Biochemistry and Molecular Biophysics); Cell Biology; Urinary System (Chemical Coordination and Homeostasis); Tumor Biology

BIOSYSTEMATIC NAMES: Hominidae--Primates, Mammalia, Vertebrata, Chordata, Animalia; Muridae--Rodentia, Mammalia, Vertebrata, Chordata, Animalia

ORGANISMS: CL-1 cell line (Hominidae)--androgen-dependent, cellular properties, growth, human prostate *cancer* cells, molecular properties ; CL-2 cell line (Hominidae)--androgen-dependent, cellular properties, growth, human prostate *cancer* cells, molecular properties; LNCaP cell line (Hominidae)--androgen-dependent, cellular properties, growth, human prostate *cancer* cells, molecular properties; mouse (Muridae

BIOSYSTEMATIC CLASSIFICATION (SUPER TAXA): Animals; Chordates; Humans; Mammals; Nonhuman Mammals; Nonhuman Vertebrates; Primates; Rodents; Vertebrates

DISEASES: prostate *cancer*--hormone refractory, metastatic, neoplastic disease, reproductive system disease/male, urologic disease

CHEMICALS & BIOCHEMICALS: *E-cadherin*--*downregulation*; basic fibroblast growth factor--messenger RNA, overexpression; bcl-2--

messenger RNA, overexpression; caveolin--messenger RNA, overexpression ; epidermal growth factor receptor--messenger RNA, overexpression; etoposide--antineoplastic-drug; interleukin-6--messenger RNA, overexpression; interleukin-8--messenger RNA, overexpression; p53--*downregulation*; paclitaxel {Taxol}--antineoplastic-drug; pentaerythritol tetranitrate--*downregulation*; transforming growth factor-beta--messenger RNA, overexpression; vascular endothelial growth factor--messenger RNA, overexpression; vinblastine--antineoplastic-drug

METHODS & EQUIPMENT: semiquantitative reverse transcriptase-polymerase chain reaction--genetic method

MISCELLANEOUS TERMS: androgen deprivation

ALTERNATE INDEXING: Prostatic Neoplasms (MeSH)

CONCEPT CODES:

10064 Biochemical Studies-Proteins, Peptides and Amino Acids
02502 Cytology and Cytochemistry-General
02506 Cytology and Cytochemistry-Animal
02508 Cytology and Cytochemistry-Human
03502 Genetics and Cytogenetics-General
03506 Genetics and Cytogenetics-Animal
03508 Genetics and Cytogenetics-Human
10060 Biochemical Studies-General
10062 Biochemical Studies-Nucleic Acids, Purines and Pyrimidines
12512 Pathology, General and Miscellaneous-Therapy (1971-)
15504 Urinary System and External Secretions-Physiology and Biochemistry
15506 Urinary System and External Secretions-Pathology
16506 Reproductive System-Pathology
17002 Endocrine System-General
24004 Neoplasms and Neoplastic Agents-Pathology; Clinical Aspects; Systemic Effects
24008 Neoplasms and Neoplastic Agents-Therapeutic Agents; Therapy

BIOSYSTEMATIC CODES:

86215 Hominidae
86375 Muridae

22/5/3 (Item 3 from file: 5)

DIALOG(R)File 5:Biosis Previews(R)

11981435 BIOSIS NO.: 199900234748

E-cadherin expression as a marker of tumor aggressiveness in routinely processed radical prostatectomy specimens.

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SUMMARY LANGUAGE: English

ABSTRACT: Objectives. Approximately 30% of clinically localized prostate adenocarcinomas *treated* by radical prostatectomy (RP) will recur within 10 years. To prevent recurrence, new adjuvant therapies are in development that seek to *treat* high-risk patients after surgery. To identify patients as candidates for these *treatments*, improved biomarkers for predicting prognosis are needed. Reduced expression of E-cadherin has been proposed as a new marker for predicting prognosis in prostate adenocarcinoma. Since few studies have examined the relation between risk factors for disease progression and E-cadherin expression using routinely processed RP specimens, we used RP specimens to correlate *downregulation* of E-cadherin and pathologic stage at RP. Methods. Primary adenocarcinomas (n = 76) from formalin-fixed and

paraffin-embedded RP specimens were evaluated by immunohistochemistry against E-cadherin (HECD-1) using heat-induced epitope retrieval and automated staining (BioTek Solutions). Normal appearing prostate epithelium was used as an internal control for each specimen. Staining was scored as an estimate of the percentage of tumor cells in each specimen that showed strong plasma membrane staining. Results. Specimens were divided into three categories with respect to Gleason score: intermediate (score 5 to 6, n = 31), intermediate to high (score 7, n = 25), and high (score 8 to 9, n = 20). For pathologic stage, specimens were divided into three categories: low stage/organ confined (pT2, n = 30), intermediate stage/limited extraprostatic extension (pT3a, n = 25), and high stage/seminal vesicle-pelvic lymph node metastases (pT3b-any pTN 1, n = 21). In univariate analysis, reduced levels of E-cadherin correlated with advanced Gleason score (P = 0.003) and advanced pathologic stage (P = 0.008). In multivariate analysis, E-cadherin, preoperative prostate-specific antigen, and Gleason score all contributed independently to the prediction of high-stage disease (P <0.0001). Ten pelvic lymph node metastases from this same patient cohort were stained for E-cadherin. All were positive and 9 of 10 were moderately to strongly positive. Conclusions. Since essentially all patients in the high-stage category have a very high likelihood of disease recurrence, we conclude that the study of E-cadherin in a prospective manner as a potential biomarker of disease progression in patients with clinically organ-confined prostate *cancer* who undergo RP is warranted. Additionally, our finding that most metastatic tumor cells in pelvic lymph nodes express E-cadherin supports the notion that the establishment of the distant colonization and growth of metastatic tumor cells may be facilitated by expression or re-expression of previously downregulated E-cadherin. This would strongly suggest that irreversible genetic inactivation through mutation or allelic loss at 16q2.3 is probably not the mechanism of E-cadherin *downregulation* in most abnormally expressing primary prostate carcinomas.

DESCRIPTORS:
MAJOR CONCEPTS: Tumor Biology
BIOSYSTEMATIC NAMES: Hominidae--Primates, Mammalia, Vertebrata, Chordata, Animalia
ORGANISMS: human (Hominidae)--male, patient
BIOSYSTEMATIC CLASSIFICATION (SUPER TAXA): Animals; Chordates; Humans; Mammals; Primates; Vertebrates
DISEASES: prostate *cancer*--neoplastic disease, tumor aggressiveness, surgical *treatment*, urologic disease, reproductive system disease/male
CHEMICALS & BIOCHEMICALS: *E-cadherin*--tumor aggressiveness marker, tumor specimen expression
METHODS & EQUIPMENT: radical prostatectomy--surgical method
ALTERNATE INDEXING: Prostatic Neoplasms (MeSH)
CONCEPT CODES:
24006 Neoplasms and Neoplastic Agents-Biochemistry
11105 Anatomy and Histology, General and Comparative-Surgery
13004 Metabolism-Carbohydrates
13012 Metabolism-Proteins, Peptides and Amino Acids
24008 Neoplasms and Neoplastic Agents-Therapeutic Agents; Therapy
16506 Reproductive System-Pathology
15506 Urinary System and External Secretions-Pathology
01056 Microscopy Techniques-Histology and Histochemistry
24007 Neoplasms and Neoplastic Agents-Carcinogens and Carcinogenesis
10064 Biochemical Studies-Proteins, Peptides and Amino Acids
16501 Reproductive System-General; Methods
15501 Urinary System and External Secretions-General; Methods
12512 Pathology, General and Miscellaneous-Therapy (1971-)
11108 Anatomy and Histology, General and Comparative-Microscopic and Ultramicroscopic Anatomy
10068 Biochemical Studies-Carbohydrates
BIOSYSTEMATIC CODES:
86215 Hominidae
?ds

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Set     Items   Description
S1       3306   E-CADHERIN
S2          0   S1 AND ENDOTHELIN B RECEPTOR
S3      16499   CATENIN?
S4       1160   S3 AND S1
S5       4105   ENDOTHELIN B RECEPTOR
S6          0   S5 AND S4
S7       1040   S1 AND CANCER?
S8          0   S7 AND S5
S9          0   S7 AND ENDOTHELIAN ANTAGONIST?
S10      3690   SY AND TREAT?
S11       132   S7 AND TREAT?
S12         0   S11 AND BQ788
S13       901   BQ788
S14         0   S13 AND S1
S15         1   S13 AND S3
S16         0   S7 AND ENDOTHELIN
S17         0   S7 AND ENDOTHELIN RECEPTOR?
S18       132   S7 AND TREAT?
S19         4   S18 AND MELANOMA
S20         2   RD (unique items)
S21         6   S18 AND DOWNREGULATION
S22         3   RD (unique items)
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               0  ADMINISTER COMPOUND
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     S24       0  S18 AND ADMINISTER?
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